


PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

(Chapter II of the Patent Cooperation Treaty)

(PCT Article 36 and Rule 70)

| | | | |
|---|--|--|--|
| Applicant's or agent's file reference P200302806PC | | FOR FURTHER ACTION | See Form PCT/PEA/416 |
| International application No. PCT/ES2004/000511 | | International filing date (day/month/year) 17.11.2004 | Priority date (day/month/year) 28.11.2003 |
| International Patent Classification (IPC) or national classification and IPC C07C401/00 | | | |
| Applicant LABORATORIOS VINAS S.A. et al. | | | |
| <p>1. This report is the international preliminary examination report, established by this International Preliminary Examining Authority under Article 35 and transmitted to the applicant according to Article 36.</p> <p>2. This REPORT consists of a total of 6 sheets, including this cover sheet.</p> <p>3. This report is also accompanied by ANNEXES, comprising:</p> <p>a. <input checked="" type="checkbox"/> sent to the applicant and to the International Bureau a total of 1 sheets, as follows:</p> <p><input type="checkbox"/> sheets of the description, claims and/or drawings which have been amended and are the basis of this report and/or sheets containing rectifications authorized by this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions).</p> <p><input type="checkbox"/> sheets which supersede earlier sheets, but which this Authority considers contain an amendment that goes beyond the disclosure in the international application as filed, as indicated in item 4 of Box No. I and the Supplemental Box.</p> <p>b. <input type="checkbox"/> (sent to the International Bureau only) a total of (indicate type and number of electronic carrier(s)) , containing a sequence listing and/or tables related thereto, in computer readable form only, as indicated in the Supplemental Box Relating to Sequence Listing (see Section 802 of the Administrative Instructions).</p> | | | |
| <p>4. This report contains indications relating to the following items:</p> <p><input checked="" type="checkbox"/> Box No. I Basis of the opinion</p> <p><input type="checkbox"/> Box No. II Priority</p> <p><input checked="" type="checkbox"/> Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability</p> <p><input type="checkbox"/> Box No. IV Lack of unity of invention</p> <p><input checked="" type="checkbox"/> Box No. V Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement</p> <p><input type="checkbox"/> Box No. VI Certain documents cited</p> <p><input type="checkbox"/> Box No. VII Certain defects in the international application</p> <p><input type="checkbox"/> Box No. VIII Certain observations on the international application</p> | | | |
| Date of submission of the demand 13.06.2005 | | Date of completion of this report 30.03.2006 | |
| Name and mailing address of the international preliminary examining authority:  European Patent Office D-80298 Munich Tel. +49 89 2399 - 0 Tx: 523656 epmu d Fax: +49 89 2399 - 4465 | | Authorized Officer Goetz, G Telephone No. +49 89 2399-8105 | |



**INTERNATIONAL PRELIMINARY REPORT
ON PATENTABILITY**

10/579594

International application No.
PCT/ES2004/000511

AP20R0001PCT/70 17 MAY 2006

Box No. I Basis of the report

1. With regard to the **language**, this report is based on the international application in the language in which it was filed, unless otherwise indicated under this item.
 - ☐ This report is based on translations from the original language into the following language , which is the language of a translation furnished for the purposes of:
 - ☐ international search (under Rules 12.3 and 23.1(b))
 - ☐ publication of the international application (under Rule 12.4)
 - ☐ international preliminary examination (under Rules 55.2 and/or 55.3)
2. With regard to the **elements*** of the international application, this report is based on (*replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report*):

Description, Pages

1-18 as originally filed

Claims, Numbers

4-22 as originally filed

1-3 filed with telefax on 10.11.2005

- ☐ a sequence listing and/or any related table(s) - see Supplemental Box Relating to Sequence Listing
3. ☐ The amendments have resulted in the cancellation of:
 - ☐ the description, pages
 - ☐ the claims, Nos.
 - ☐ the drawings, sheets/figs
 - ☐ the sequence listing (*specify*):
 - ☐ any table(s) related to sequence listing (*specify*):
 4. ☐ This report has been established as if (some of) the amendments annexed to this report and listed below had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the Supplemental Box (Rule 70.2(c)).
 - ☐ the description, pages
 - ☐ the claims, Nos.
 - ☐ the drawings, sheets/figs
 - ☐ the sequence listing (*specify*):
 - ☐ any table(s) related to sequence listing (*specify*):

* If item 4 applies, some or all of these sheets may be marked "superseded."

**INTERNATIONAL PRELIMINARY REPORT
ON PATENTABILITY**

International application No.
PCT/ES2004/000511

Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

1. The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non-obvious), or to be industrially applicable have not been examined in respect of:

- ☐ the entire international application,
☒ claims Nos. 1-2,4-6,9-22 (all in part)

because:

- ☐ the said international application, or the said claims Nos. relate to the following subject matter which does not require an international preliminary examination (specify):
☒ the description, claims or drawings (*indicate particular elements below*) or said claims Nos. 1-2,4-6,9-22 (all in part) are so unclear that no meaningful opinion could be formed (*specify*):

see separate sheet

- ☐ the claims, or said claims Nos. are so inadequately supported by the description that no meaningful opinion could be formed.
- ☐ no international search report has been established for the said claims Nos.
- ☐ the nucleotide and/or amino acid sequence listing does not comply with the standard provided for in Annex C of the Administrative Instructions in that:
- | | |
|----------------------------|--|
| the written form | <input type="checkbox"/> has not been furnished |
| | <input type="checkbox"/> does not comply with the standard |
| the computer readable form | <input type="checkbox"/> has not been furnished |
| | <input type="checkbox"/> does not comply with the standard |
- ☐ the tables related to the nucleotide and/or amino acid sequence listing, if in computer readable form only, do not comply with the technical requirements provided for in Annex C-*bis* of the Administrative Instructions.
- ☐ See separate sheet for further details

**INTERNATIONAL PRELIMINARY REPORT
ON PATENTABILITY**

International application No.
PCT/ES2004/000511

Box No. V Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

| | | |
|-------------------------------|-------------|-------|
| Novelty (N) | Yes: Claims | 3,7,8 |
| | No: Claims | |
| Inventive step (IS) | Yes: Claims | 3,7,8 |
| | No: Claims | |
| Industrial applicability (IA) | Yes: Claims | 3,7,8 |
| | No: Claims | |

2. Citations and explanations (Rule 70.7):

see separate sheet

**INTERNATIONAL PRELIMINARY
REPORT ON PATENTABILITY
(SEPARATE SHEET)**

International application No.

PCT/ES2004/000511

D1: WO 92 03414 A1

D2: EP-A1-0 078 704

According to Rule 66.4(b) PCT the International Preliminary Examining Authority may give the applicant one or more additional opportunities to submit amendments or arguments.

This rule applies to amendments or arguments. The treatment of different requests (main and auxiliary requests), however, is not foreseen under the PCT.

Since the applicant has had one additional opportunity to submit amendments or arguments (main request), present examination is done for the main request filed with fax dated 10-11-2005.

Re item III

1. Present claims 1 to 2, 4 to 6 and 9 to 22 are not considered to meet the requirements of Article 6 PCT:

In these claims "W" is defined as being "a diacylazo group such as 4-phenyl-1,2,4-triazolin-3,5-dione or phthalazin-1,4-dione". This definition is not clear:

it is not unambiguously clear how such a group is attached or integrated into the given ring system since no information is given in the application documents as filed.

Re item V

1. The compounds according to present claims 3, 7 and 8 differ from the compounds disclosed in D1 and D2 by the fact that the claimed compounds have a mono-halo-vinyl-group attached to C-20 whereas the prior art only discloses compounds having a di-halo-vinyl-group at this position.
Due to this difference novelty of the claimed compounds is established.
The subject matter of present claims 3, 7 and 8 (compounds) as well as claims 4 to 6 (compounds), and 9 to 21 (process for preparing these compounds) insofar as "W" has the meaning of "SO₂" is thus novel over said prior art (PCT Article 33.2).
2. The presently claimed compounds which are considered to be novel, are useful as

starting compounds for preparing vitamin D derivatives.

Since the compounds disclosed in D1 and D2 are used for the same purpose these documents are considered to represent the closest prior art.

The prior art compounds, however, show the disadvantage that due to the presence of a dihalovinyl-group their preparation is difficult and when used to prepare vitamin D derivatives it is difficult to obtain end-products where the alkene-group attached to C-20 has no halogen atom any more.

Having regard to this prior art the underlying problem can be defined by the provision of further compounds which can be used for the preparation of biologically active vitamin D derivatives not showing these disadvantages.

The claimed compounds solve this problem as shown in the examples.

In the absence of any indication or hint in the prior art the claimed compounds are considered to be based on an inventive step. In addition a further advantage can be seen in the fact that stereo selectivity is improved and fewer side-products and impurities are obtained.

The subject matter of present claims 3,7,8 as well as claims 4 to 6 and 9 to 21 insofar as "W" has the meaning of "SO₂" is thus considered to be based on an inventive step having regard to the prior art disclosed in D1 and D2 (PCT Article 33.3).

3. Present claim 22 is not considered to be based on an inventive step (PCT Article 33.3):

The use of an aldehyde according to formula (VI) in the preparation of compounds according to present formula (I) is already disclosed in D1 (see schemes 1 and 2).

The presently claimed use is therefore considered to represent an obvious alternative which is not based on an inventive step: the skilled person would certainly use such an aldehyde for the preparation of compounds according to formula (I) when confronted with the problem to prepare compounds according to formula(I).

In particular D1 teaches that the process of D1 can be used for iodinated, brominated and chlorinated products which corresponds to those compounds of present application where "X" represents chlorine, bromine or iodine.

The use according to present claim 22 is thus considered not to be based on an inventive step (PCT Article 33.3).

3. Industrial applicability is given for claims 3 to 22 (PCT Article 33.4)

28/5/9594

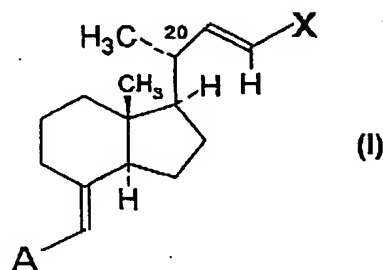
Main request

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AP20 Rec'd PCT/PTO 17 MAY 2006

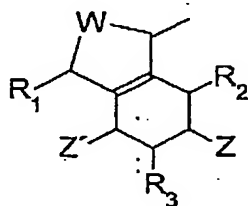
CLAIMS

1. A compound of general formula (I)

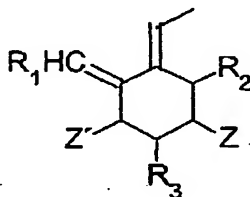


wherein:

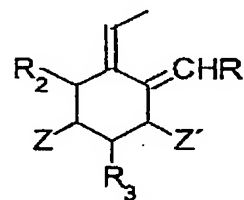
- X represents a halogen atom selected from chlorine, bromine and iodine and
- A is selected from any of the moieties corresponding to general formulas (A1), (A2) and (A3)



(A1)



(A2)



(A3)

in which:

- Z and Z' are independently selected from hydrogen, a hydroxyl group and an -OR protected hydroxyl group, where R is a hydroxyl protective group;
- W represents a dienophile selected from SO₂ and a diacylazo group such as 4-phenyl-1,2,4-triazolin-3,5-dione or phthalazin-1,4-dione; and
- R₁, R₂ and R₃ are independently selected from hydrogen, halogen, a hydroxyl group, an -OR protected hydroxyl group, wherein R is a hydroxyl protective group, C₁-C₆ alkyl or C₁-C₆ alkenyl, optionally substituted with halogen, hydroxyl, cyano or amino, or a dialkyl(C₁-C₅) ether or alkyl(C₁-C₅) amino group.

2. A compound according to claim 1, wherein X is an iodine atom.

3. A compound according to any of claims 1 or 2, wherein W is the SO₂ group.